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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,061	03/09/2005	Oliver May	266811US0XPCT	4748

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EXAMINER

MEAH, MOHAMMAD Y

ART UNIT	PAPER NUMBER
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1652

SHORTENED STATUTORY PERIOD OF RESPONSE	NOTIFICATION DATE	DELIVERY MODE
3 MONTHS	04/20/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

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Office Action Summary	Application No.	Applicant(s)	
	10/527,061	MAY ET AL.	
	Examiner	Art Unit	
	Mohammad Meah	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 January 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 10-21 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 10-21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Claims 1-9 were examined in prior action. With the response filed 1/23/2007, the applicant canceled claims 1-9 and added new claims 10-21.

Priority

Acknowledgement is made of applicant's PCT priority date based on application filing date of 10/15/2003 of PCT/EP03/11432 and foreign applications Germany 102-51-184.5 filed on date 11/04/2002.

Claim Rejections

35 U.S.C 112

35 U.S.C. 112 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 10-21 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 10-12- the recitation " all the identifying characteristics--- or a mutant derived therefrom" makes the claim indefinite and vague. As it is unclear what are these characteristics in all mutants.

Claims 10,12, 14, 11 (dependent on claim 10),13 (dependent on claim 10) and 15-21 (dependent on claim 14) are rejected on recitation " inactivation in *dada* or *dsdA*" as the term " inactivation in *dada* or *dsdA*" makes these claims

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indefinite and vague as it is unclear what the term "inactivation in *dada* or *dsdA*" encompasses.

35 U.S.C. 112 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10, 12, 14-19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 10 is directed to a genus of microorganism comprising any mutant derived from *E. coli* DSM 15181 comprising genes of D-amino acid oxidase and/or D-serine dehydratase inactivated by any mutagenesis, as said derived mutant necessarily does not consist of identifying characteristics of *E. coli* DSM 15181, from any source. Claim 12 is directed to a genus of microorganism comprising any mutant derived from *E. coli* DSM 15182 comprising genes of D-amino acid oxidase and/or D-serine dehydratase inactivated by any mutagenesis as said derived mutant necessarily does not consist of identifying characteristics of *E. coli* DSM 15182 from any source. Claims 14-19 are directed to process of preparing D-amino acid using a genus of transformed *E. coli* comprising any gene of D-amino acid oxidase and/or D-serine dehydratase inactivated by any

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mutagenesis from any source. The specification teaches the structure of only a few representative species of such recombinant microorganisms. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than efficient production of D-amino acids and the lack of D-amino acid oxidase and/or D-serine dehydratase activity. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 10, 12, 14-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for specific recombinant microorganism (such as *E. coli* DSM 15181 or DSM 15182) or a microorganism or mutant therefrom having identifying characteristics of *E. coli* DSM 15181 or DSM 15182 and method of production of D-amino acid using said recombinant microorganisms does not reasonably provide enablement for any recombinant microorganisms comprising any mutant derived from *E. coli* DSM 15181 or *E. coli* DSM 15181 comprising genes of D-amino acid oxidase and/or D-serine dehydratase inactivated by any mutagenesis, as said derived mutant necessarily does not consist of identifying characteristics of *E. coli* DSM 15181 or *E. coli* DSM 15181 and method of production of D-amino acid using said recombinant microorganisms. There are many ways genes of D-amino acid oxidase and/or D-serine dehydratase in a microorganisms can be inactivated such as deletion, substitution of specific amino acid residues of DNA sequence of the D-amino

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acid oxidase and/or D-serine dehydratase or deletion of the whole genes, etc.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breath of the claim(s).

Claims 10 and 12 are so broad as to encompass any recombinant microorganisms comprising any mutant derived from *E. coli* DSM 15181 or *E. coli* DSM 15182 comprising genes of D-amino acid oxidase and/or D-serine dehydratase inactivated by any mutagenesis, as said derived mutant necessarily does not consist of identifying characteristics of *E. coli* DSM 15181 or *E. coli* DSM 15182. Claims 14-19 are so broad as to encompass any method of preparing D-amino acid using any recombinant microorganism with gene any of D-amino acid oxidase and/or D-serine dehydratase inactivated by any means and method of production of D-amino acid using said recombinant microorganisms. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to any recombinant microorganism with any gene of D-amino acid oxidase and/or D-serine

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dehydratase inactivated by any means broadly encompassed by the claims. In view of the great breaths of claims 10, 12 and 14-19, amount of experimentation required to make the said mutant microorganism or any E. coli having inactivated any D-amino acid oxidase and/or D-serine dehydratase, the lack of guidance, working examples, unpredictability of the art in predicting the function from protein's structure (Whisstock, et al. Quarterly Rev. Biophy. 2003, 36, pp 307-340), the claimed invention would require undue experimentation. As such the specification fail to teach one of ordinary skill how to use the full scope of the claims.

Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to inactivation of few genes encoding mutated D-amino acid oxidase and/or D-serine dehydratase.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the

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result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass microorganisms comprising wherein microorganisms D-amino acid oxidase and/or D-serine dehydratase are inactivated by any method of mutagenesis and method of production of D-amino acid using said recombinant microorganisms because the specification does not establish: (A) regions of the protein structure which may be modified to eliminate D-amino acid oxidase activity (B) the general tolerance of modification and extent of such tolerance on D-amino acid oxidase and/or D-serine dehydratase; (C) a rational and predictable scheme for modifying any D-amino acid oxidase and/or D-serine dehydratase residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any recombinant microorganisms comprising containing genes of D-amino acid oxidase and/or D-serine dehydratase inactivated by any method of mutagenesis and method of production of D-amino acid using said recombinant microorganisms. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without

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sufficient guidance, determination of oxidoreductase variants, having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir,1988).

Conclusion

Claims 10, 12 and 14-19 are rejected and claims 11, 13 and 20-21 are allowable if they are made independent from the rejected claims and if rewritten to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.


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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mohammad Meah whose telephone number is 571-272-1261. The examiner can normally be reached on 8:30-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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